

PSJ2 Exh 1

From: Livingston, Kristin </O=ENDO PHARMACEUTICALS INC/OU=ENDO/CN=RECIPIENTS /CN=LIVINGSTON.KRISTIN>
To: Brady, Dorothy M.; Ahdieh, Harry; Gallion, Kirk; Kerwin, Rosemary; Kurkimilis, Elisabeth; Lander, MaryEllen; Livingston, Kristin; Ma, Tina; mpadams@newdrugservices.com; Platt, Rebecca; Raudenbush, MaryAlice; Smith Carliss, Richard; Tom Sciascia (E-mail); Travers, Debbie; Utecht, Ken; Wydro, Phillip
Sent: 3/25/2002 7:39:44 PM
Subject: Risk Management Presentation
Attachments: EN3202 Risk Management.ppt

Dear Claims Subteam Members:

Attached is the Risk Management presentation that was presented to the Executive Committee (from Debbie).

Kris



EN3202 Risk Management.ppt

Deb

Debbie Travers
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-----Original Message-----

From: Livingston, Kristin
Sent: Monday, March 25, 2002 10:38 AM
To: Travers, Debbie
Subject: A couple of things

Dear Debbie:

Do you still want me to try to reschedule the next EN3202/03 Subteam meeting for Friday, 4/8?

Also, just a reminder to send me the Risk Management presentation electronically so that I can send it to the rest of the Claims Subteam.

Thanks.

Kris

Produced In Native Format

Endo Risk Management Strategy

- **Global Issues**

- Receptiveness of market to potent, chronic-use opioids has been dampened because of abuse and diversion issues with Purdue's OxyContin[®], played prominently in the media
- FDA is treading water
 - No clear guidance to NDA sponsors
 - "Wait to see what they offer" approach



Physician Feedback

- **AAPM Advisory Boards – EN3202 & 3231**

- Pain specialists / Policy makers
- Clearly afraid of abuse and diversion:
 - “OxyContin® is a good drug marketed by an unethical company”
- Advised Endo to be upfront about abuse potential and proactive with programs and tools to raise comfort level of prescribers
 - Educational programs
 - Tools to identify potential abusers
 - Registry studies
- “Endo has the chance to do it right!”



EN 3202 Qualitative Market Research

- Pain specialists, PCP's, oncologists, orthopedic surgeons, rheumatologists all cite less frequent use of OxyContin® because of media attention
- Most felt that educational programs (especially for PCP's) would be helpful in easing fears of prescribing, but would not be the sole factor in deciding which drug to prescribe



Reality Check

- Endo is not the market leader
- Resources are limited relative to Purdue and Janssen

Requires selective development and implementation of high-impact, cost-effective tactics that are clearly identifiable to Endo and its educational efforts on the science of pain



Implications for ENDO

- **The premier pain management company must address abuse and diversion issues up front and proactively**
- **Endo must market new opioids responsibly and be honest about abuse potential**
- **Opportunity to partner with key pain management policy makers**



Implications for EN3202

- EN3202 has few points of distinction from OxyContin®; physicians indicate that they will probably use them interchangeably
- Potency is double-edged sword
- Fear of abuse and deterrence is one of the major barriers to rapid adoption of EN3202
- Physicians are looking for an alternative to OxyContin® because of the media attention and stigma. (Mel Gitlin – Tulane – “Doctors will prescribe this because it is not OxyContin®”)



Implications for EN 3231

- Abuse/diversion issues with EN 3231 are a concern, but to a lesser extent than with extended release formulations (e.g. OxyContin)
- Addressing the issues of abuse is a “price of entry” for EN 3231 and all new opioids
- For EN 3231, it is sufficient to be a “part” of the educational mix, not a focus
 - Primary Focus: NMDA Enhanced Analgesia and the disease of pain



Corporate Strategy

- **Establish Endo as the premier specialty pharmaceutical company and a leader in pain management**
- **Position Endo as a responsible marketer of opioid analgesics**



EN3202 Strategy

- **Differentiate EN3202 from OxyContin®**
 - Lower doses of EN3202 needed for equivalent analgesia
 - Less escalation of dose with chronic use
 - Side effects
- **Create market environment prior to launch that ensures rapid uptake and adoption of EN3202**
 - Remove barriers – real and perceived - to prescribers
 - Alignment with key thought leaders and regulatory agencies on abuse and deterrence issues



EN 3231 Strategy

- **Establish the science of NMDA-Enhanced Analgesia and link to clinical benefits**
 - pathophysiological role in the disease of pain
 - link to elimination of tolerance, opioid-sparing effects
- **Develop ample EN 3231 product champions**
 - Recognize NMDA Enhanced Analgesia as an advance
 - Perceive Endo as a trusted partner
- **Enhance the EN 3231 product profile for both prescribers and payors**
 - Expand clinical program
 - Establish a pharmacoeconomic rationale
- **Establish EN 3231 as the new standard of care for the management of mod/severe chronic pain**
 - Based upon MOA, clinical benefits, and value



EN3202

Branding/Image/ Positioning

- **Branding not yet determined**
- **Positioning research underway**
 - Likely use in severe pain
 - Cancer
 - Severe OA
 - Severe back pain
 - Niches – Sickle Cell Disease / Interstitial Cystitis
 - Pain Specialists and Oncologists seem most receptive to product profile, but are clearly concerned about abuse and diversion
 - Topic comes up unaided in every interview as soon as potency and extended release are mentioned



EN 3231

Branding/Image/Positioning

- **The branding for EN 3231 is still under development**
 - Unique feeling proposition: ***A Charismatic Agent of Change***
 - Pre-launch scientific exhibit reflects a "***new day***" in pain management
- **Preliminary Positioning (research ongoing)**
 - Target Audiences:
 - Pain Specialists, Oncologists, and PCP's and select others who prescribe opioids
 - Positioning Concept:
 - EN 3231 is the ***first and only opioid analgesic to provide NMDA receptor antagonism*** and is the new standard of care for the management of moderate to severe chronic pain
 - Customer Benefit:
 - EN 3231 will empower physicians to offer their patients the pain relief they need over the long-term to live happier, more productive lives



Key Messages for EN3202

- **Potent extended release opioids are an essential tool in the armamentarium of pain management**
- **EN3202 is a better alternative to OxyContin®**
 - Provides better control of pain at lower mg doses
 - Can be used for extended periods of time safely
 - EN3202 is part of the Endo oxymorphone family of products which have been safely used for treatment of pain for more than 40 years
- **EN3202 has the potential for abuse and diversion**
- **Endo works with the pain management community to develop educational programs and tools which help the prescribing physician to:**
 - Target appropriate patients
 - Recognize high risk patients
 - Recognize signs of abuse and diversion



EN 3231

Key Messages/Reasons to Believe

- **EN 3231 prevents the activation of the NMDA receptor, which when activated plays an important role in the development of chronic and/or refractory pain**
- **Opioid-sparing: lower dose vs. traditional opioids to achieve necessary pain relief**
- **Tolerance: Unlike traditional opioids, little/no need to increase dose over time to achieve the same level of pain relief**
- **Reduced need for rescue medication compared to traditional opioids**
- **Significantly higher patient satisfaction (60% vs. 12% pre-study opioids)**
- **Well-tolerated with no “new” side effects and no dose-dependent side effects**

Risk Management: Advocating the appropriate use of opioids

- Opioids are an important and necessary for million of patients with pain
- However, potential for abuse/diversion exists w/all opioids, including EN 3231
- Endo is committed to working with the pain management community to develop educational programs and tools which help the prescribing physician to:
 - Target appropriate patients
 - Recognize high risk patients
 - Recognize signs of abuse and diversion



ROI for EN3202

- **Potential sales of EN3202 depend directly on prescribers' comfort level with risk of abuse and diversion**
- **Current preliminary forecast estimates potential sales of \$275-340MM**
- **Endo's revenues will be 50% of total sales due to partnership with Penwest**
- **Risk management tactics will have to be leveraged across other products to provide adequate ROI (EN3231/Percocet/Dex's)**



ROI for EN 3231

- **Commercial potential is most dependent on the level of acceptance of the science of NMDA Enhanced Analgesia**
 - Linked to clinical benefits and EN 3231
- **Prescribers' comfort level with risk of abuse and diversion represents a relatively smaller risk to EN 3231 and is more closely correlated with risks generalized to opioids in general**
- **Current preliminary forecast estimates potential peak sales of \$450-500MM**
- **Risk management tactics will be incorporated as one part of larger marketing programs (e.g. symposia, CME)**



Timing

- **Pre-launch**

- Cultivate relationships with thought leaders who are well respected in the area of abuse and addiction (Portnoy/Passick)
- Incorporate risk management messages into all educational programs, but not as primary focus
- Develop tools which help the prescriber detect abuse and diversion
- Seek a seat at the policy making tables of key pain management organizations



Timing

- **Post Launch**

- Comply with the FDA's requirements for post marketing safety surveillance
- Roll out educational and patient tracking tools
- Be very visible as the "responsible marketer" of opioid analgesics with a proactive public relations campaign



Market Research

- **Abuse, addiction and diversion issues need to be explored with potential prescribers**
 - Routine agenda item at all advisory boards
 - (If we don't bring it up, they will)
 - Probe on effectiveness of Purdue program
 - Integral part of demand and positioning research
 - Thorough analysis and evaluation of existing high-profile competitor programs (e.g. Purdue's Partners Against Pain as well as others)



Risk Management Musts

- **Satisfy FDA Requirements**
 - Post marketing safety surveillance
 - Educational programs on appropriate use of EN3202 for physicians who prescribe
 - Appropriate positioning and promotion of EN3202



Endo Late-Stage Opioids Risk Management Tactics

- **Pre-Marketing**

- Align with thought leaders and organizations who are interested in teaching appropriate use of strong opioid analgesics
- Inclusion of risk management message
 - EN 3202: all presentations
 - EN 3231: part of larger symposia
- Develop tools which help physicians identify high risk patients and recognize signs and behaviors associates with abuse and diversion (i.e., SOAP)



Endo Late-Stage Opioids Risk Management Tactics

- **Launch**

- Sales force trained on abuse and diversion issues and appropriate use for chronic pain
- Proactive roll out of educational programs and patient management tools (Avoid perception that this has been mandated by FDA/DEA)
- Abuse and diversion message for sales force
 - Balanced approach in all EN3202 details
 - Avoid claims of “less abuse potential” and focus on ability to use lower doses of opioid



Endo Risk Management Key Tactics

- **SOAP**
 - **Screening for Opioid Addiction Potential**
 - Questionnaire tool for assessing a patient's potential for developing addictive and drug seeking behaviors
 - Being developed in conjunction with NIH and NIDA by Inflexxion
- **Patient Registry**
 - **Prospective data collection on patient use of opioids, diseases being treated, patient satisfaction, etc. (Real world use of opioids)**
- **Endo Center for Pain Management**
 - **800 END-PAIN**
 - Support for product and general questions
 - Access to recognized guidelines
- **Patient Profiles in Pain**
 - Visualize the variety of situations encountered to advance assessment and management of Pain
 - Amortize through website, personal promotion, physician/patient brochures, symposia

